Point of Contact:
Thomas G. Larson, Ph.D.
703-308-7309
CM1, Rm. 6 B 01

```
=> FILE MEDLINE
FILE 'MEDLINE' ENTERED AT 14:34:55 ON 10 APR 2002

 FILE LAST UPDATED: 9 APR 2002 (20020409/UP). FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week. A new current-awareness alert
 frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index. See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> D QUE L10
L1         26300 SEA FILE=MEDLINE ABB=ON  PLU=ON  GENETIC VECTORS/CT
L2         80395 SEA FILE=MEDLINE ABB=ON  PLU=ON  RETROVIRIDAE+NT/CT
L3        127552 SEA FILE=MEDLINE ABB=ON  PLU=ON  RETROVIRIDAE INFECTIONS+NT/CT

L4        176412 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2 OR L3
L5          4761 SEA FILE=MEDLINE ABB=ON  PLU=ON  L1 AND L4
L6         51226 SEA FILE=MEDLINE ABB=ON  PLU=ON  DNA, VIRAL/CT
L7           351 SEA FILE=MEDLINE ABB=ON  PLU=ON  L5 AND L6
L8          1897 SEA FILE=MEDLINE ABB=ON  PLU=ON  VIRAL INTERFERENCE/CT
L9             2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L7 AND L8
L10            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L9 NOT  ECOTROPIC MURINE
                   LEUKEMIA/TI


=> D QUE L13
L1         26300 SEA FILE=MEDLINE ABB=ON  PLU=ON  GENETIC VECTORS/CT
L2         80395 SEA FILE=MEDLINE ABB=ON  PLU=ON  RETROVIRIDAE+NT/CT
L3        127552 SEA FILE=MEDLINE ABB=ON  PLU=ON  RETROVIRIDAE INFECTIONS+NT/CT

L4        176412 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2 OR L3
L5          4761 SEA FILE=MEDLINE ABB=ON  PLU=ON  L1 AND L4
L6         51226 SEA FILE=MEDLINE ABB=ON  PLU=ON  DNA, VIRAL/CT
L7           351 SEA FILE=MEDLINE ABB=ON  PLU=ON  L5 AND L6
L11         2793 SEA FILE=MEDLINE ABB=ON  PLU=ON  RNA, CATALYTIC/CT
L12            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L7 AND L11
L13            4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L12 NOT INCREASED TITER/TI


=> D QUE L16
L1         26300 SEA FILE=MEDLINE ABB=ON  PLU=ON  GENETIC VECTORS/CT
L2         80395 SEA FILE=MEDLINE ABB=ON  PLU=ON  RETROVIRIDAE+NT/CT
L3        127552 SEA FILE=MEDLINE ABB=ON  PLU=ON  RETROVIRIDAE INFECTIONS+NT/CT

L4        176412 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2 OR L3
L5          4761 SEA FILE=MEDLINE ABB=ON  PLU=ON  L1 AND L4
```

```
L11          2793 SEA FILE=MEDLINE ABB=ON  PLU=ON  RNA, CATALYTIC/CT
L14        151869 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIVIRAL AGENTS+NT/CT
L15            75 SEA FILE=MEDLINE ABB=ON  PLU=ON  L5 AND L11
L16             5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L15 AND L14


=> D QUE L19
L1           26300 SEA FILE=MEDLINE ABB=ON  PLU=ON  GENETIC VECTORS/CT
L6           51226 SEA FILE=MEDLINE ABB=ON  PLU=ON  DNA, VIRAL/CT
L17             42 SEA FILE=MEDLINE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                   VECTOR#
L18             29 SEA FILE=MEDLINE ABB=ON  PLU=ON  L17 AND L1
L19              0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L18 AND L6


=> D QUE L20
L1           26300 SEA FILE=MEDLINE ABB=ON  PLU=ON  GENETIC VECTORS/CT
L11           2793 SEA FILE=MEDLINE ABB=ON  PLU=ON  RNA, CATALYTIC/CT
L17             42 SEA FILE=MEDLINE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                   VECTOR#
L18             29 SEA FILE=MEDLINE ABB=ON  PLU=ON  L17 AND L1
L20              1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L18 AND L11


=> D QUE L21
L8            1897 SEA FILE=MEDLINE ABB=ON  PLU=ON  VIRAL INTERFERENCE/CT
L17             42 SEA FILE=MEDLINE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                   VECTOR#
L21              1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L8 AND L17


=> D QUE L22
L6           51226 SEA FILE=MEDLINE ABB=ON  PLU=ON  DNA, VIRAL/CT
L17             42 SEA FILE=MEDLINE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                   VECTOR#
L22              1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L17 AND L6


=> S L10 OR L13 OR L16 OR L19 OR L20 OR L21 OR L22
L106            12 L10 OR L13 OR L16 OR L19 OR L20 OR L21 OR L22

=> FILE EMBASE
FILE 'EMBASE' ENTERED AT 14:36:47 ON 10 APR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

 FILE COVERS 1974 TO 4 Apr 2002 (20020404/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> D QUE L44
L25             64 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS VECTOR/CT
L26           5395 SEA FILE=EMBASE ABB=ON  PLU=ON  CLONING VECTOR+NT/CT
L27           4830 SEA FILE=EMBASE ABB=ON  PLU=ON  EXPRESSION VECTOR/CT
L30           1151 SEA FILE=EMBASE ABB=ON  PLU=ON  HELPER VIRUS
L37             38 SEA FILE=EMBASE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                   VECTOR#
L38          10144 SEA FILE=EMBASE ABB=ON  PLU=ON  (L25 OR L26 OR L27)
```

```
L43          54 SEA FILE=EMBASE ABB=ON  PLU=ON  L38 AND L30
L44           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L43 AND L37


=> D QUE L51
L25          64 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS VECTOR/CT
L26        5395 SEA FILE=EMBASE ABB=ON  PLU=ON  CLONING VECTOR+NT/CT
L27        4830 SEA FILE=EMBASE ABB=ON  PLU=ON  EXPRESSION VECTOR/CT
L31        2173 SEA FILE=EMBASE ABB=ON  PLU=ON  RIBOZYME/CT
L32        3602 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTISENSE OLIGONUCLEOTIDE/CT
L33        2209 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTISENSE OLIGODEOXYNUCLEOTIDE/
                CT
L38       10144 SEA FILE=EMBASE ABB=ON  PLU=ON  (L25 OR L26 OR L27)
L40        7751 SEA FILE=EMBASE ABB=ON  PLU=ON  (L31 OR L32 OR L33)
L41         146 SEA FILE=EMBASE ABB=ON  PLU=ON  L38 AND L40
L48       16543 SEA FILE=EMBASE ABB=ON  PLU=ON  VIRUS DNA/CT
L51           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L41 AND L48


=> D QUE L54
L25          64 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS VECTOR/CT
L36         308 SEA FILE=EMBASE ABB=ON  PLU=ON  VIRUS INTERFERENCE/CT
L54           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L25 AND L36


=> D QUE L55
L25          64 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS VECTOR/CT
L37          38 SEA FILE=EMBASE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                VECTOR#
L55           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L25 AND L37


=> D QUE L56
L37          38 SEA FILE=EMBASE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                VECTOR#
L48       16543 SEA FILE=EMBASE ABB=ON  PLU=ON  VIRUS DNA/CT
L56           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L37 AND L48


=> D QUE L58
L31        2173 SEA FILE=EMBASE ABB=ON  PLU=ON  RIBOZYME/CT
L32        3602 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTISENSE OLIGONUCLEOTIDE/CT
L33        2209 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTISENSE OLIGODEOXYNUCLEOTIDE/
                CT
L37          38 SEA FILE=EMBASE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                VECTOR#
L40        7751 SEA FILE=EMBASE ABB=ON  PLU=ON  (L31 OR L32 OR L33)
L58           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L37 AND L40


=> D QUE L60
L30        1151 SEA FILE=EMBASE ABB=ON  PLU=ON  HELPER VIRUS
L37          38 SEA FILE=EMBASE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                VECTOR#
L60           2 SEA FILE=EMBASE ABB=ON  PLU=ON  L37 AND L30


=> D QUE L62
L28       76379 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS+NT/CT
L29       93327 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS INFECTION+NT/CT
```

```
L37          38 SEA FILE=EMBASE ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                VECTOR#
L39      145013 SEA FILE=EMBASE ABB=ON  PLU=ON  L28 OR L29
L61           6 SEA FILE=EMBASE ABB=ON  PLU=ON  L37 AND L39
L62           3 SEA FILE=EMBASE ABB=ON  PLU=ON  L61 NOT ADENOVIRUS/TI


=> D QUE L66
L25          64 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS VECTOR/CT
L26        5395 SEA FILE=EMBASE ABB=ON  PLU=ON  CLONING VECTOR+NT/CT
L27        4830 SEA FILE=EMBASE ABB=ON  PLU=ON  EXPRESSION VECTOR/CT
L38       10144 SEA FILE=EMBASE ABB=ON  PLU=ON  (L25 OR L26 OR L27)
L66           3 SEA FILE=EMBASE ABB=ON  PLU=ON  L38 AND (CONDITION? REPLICAT?/T
                I)


=> D QUE L68
L25          64 SEA FILE=EMBASE ABB=ON  PLU=ON  RETROVIRUS VECTOR/CT
L26        5395 SEA FILE=EMBASE ABB=ON  PLU=ON  CLONING VECTOR+NT/CT
L27        4830 SEA FILE=EMBASE ABB=ON  PLU=ON  EXPRESSION VECTOR/CT
L38       10144 SEA FILE=EMBASE ABB=ON  PLU=ON  (L25 OR L26 OR L27)
L64          82 SEA FILE=EMBASE ABB=ON  PLU=ON  CONDITION? REPLICAT?
L67        2275 SEA FILE=EMBASE ABB=ON  PLU=ON  L38(MAJ)
L68           2 SEA FILE=EMBASE ABB=ON  PLU=ON  L67 AND L64
```

index as major focus of document.

```
=> S L56 OR L60 OR L62 OR L66 OR L68
L107          8 L56 OR L60 OR L62 OR L66 OR L68

=> FILE HCAPLUS
FILE 'HCAPLUS' ENTERED AT 14:39:16 ON 10 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 10 Apr 2002  VOL 136 ISS 15
FILE LAST UPDATED: 8 Apr 2002  (20020408/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the CAS files between 12/27/01
and 1/23/02.  As of 1/23/02, the situation has been resolved.  Searches
```

and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

```
=> D QUE L78
L69        2338 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RETROVIRAL VECTORS/CT
L76         364 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CONDITION? (3W) REPLICAT?
L77           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L69 AND L76
L78           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L77 NOT HAPTEN-COAGULATION
                AGENT/TI


=> D QUE L82
L71        5725 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RIBOZYMES+NT/CT
L72        4967 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTISENSE OLIGONUCLEOTIDES+OLD
                /CT
L73        3031 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTISENSE RNA+OLD/CT
L74        2830 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTISENSE DNA+OLD/CT
L76         364 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CONDITION? (3W) REPLICAT?
L80       14918 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L71 OR L72 OR L73 OR L74)
L81           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L80 AND L76
L82           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L81 NOT (HAPTEN-COAGULATION
                AGENT OR TELOMERASE COMPONENTS)/TI


=> D QUE L84
L75       16383 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIVIRAL AGENTS+NT/CT
L76         364 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CONDITION? (3W) REPLICAT?
L83           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND L76
L84           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 NOT (BLEOMYCIN OR
                INTERLEUKIN)/TI


=> D QUE L88
L86          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (CONDITION? AND REPLICAT? AND
                (VIRUS OR VIRAL) AND VECTOR#)/TI
L88           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L86 NOT (HERPES OR ADENO-ASSOC
                IATED OR ADENOVIRUS)/TI


=> S L78 OR L82 OR L84 OR L88
L108          8 L78 OR L82 OR L84 OR L88

=> FILE BIOTECHNO
FILE 'BIOTECHNO' ENTERED AT 14:41:38 ON 10 APR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE LAST UPDATED: 09 APR 2002      <20020409/UP>
FILE COVERS 1980 TO DATE.

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<

=> D QUE L91
L89          37 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  CONDITION? (5A) REPLICA?
                (5A) VECTOR#
L90       34789 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  IMMUNODEFICIENCY OR HIV
L91           4 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L89 AND L90
```

```
=> D QUE L93
L89          37 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  CONDITION? (5A) REPLICA?
                (5A) VECTOR#
L92        2068 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  RIBOZYME#
L93           1 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L89 AND L92


=> S L91 OR L93
L109          4 L91 OR L93

=> FILE BIOTECHDS
FILE 'BIOTECHDS' ENTERED AT 14:42:24 ON 10 APR 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD AND INSTITUTE FOR SCIENTIFIC INFORMATION

FILE LAST UPDATED: 03 APR 2002      <20020403/UP>
>>> SDI'S MAY BE RUN WEEKLY OR EVERY TWO WEEKS NOW.
    (EVERY TWO WEEKS IS THE DEFAULT).
    FOR PRICING INFORMATION  SEE HELP COST  <<<

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<

=> D QUE L97
L94          33 SEA FILE=BIOTECHDS ABB=ON  PLU=ON  CONDITION? (5A) REPLICA?
                (5A) VECTOR#
L95        5203 SEA FILE=BIOTECHDS ABB=ON  PLU=ON  IMMUNODEFICIENCY OR HIV
L96           8 SEA FILE=BIOTECHDS ABB=ON  PLU=ON  L94 AND L95
L97           6 SEA FILE=BIOTECHDS ABB=ON  PLU=ON  L96 NOT (EXON AMPLIFICATION
                OR ADENO VIRUS)/TI


=> D QUE L99
L94          33 SEA FILE=BIOTECHDS ABB=ON  PLU=ON  CONDITION? (5A) REPLICA?
                (5A) VECTOR#
L98        1659 SEA FILE=BIOTECHDS ABB=ON  PLU=ON  RIBOZYME
L99           3 SEA FILE=BIOTECHDS ABB=ON  PLU=ON  L94 AND L98


=> S L97 OR L99
L110          6 L97 OR L99

=> FILE WPIDS
FILE 'WPIDS' ENTERED AT 14:43:39 ON 10 APR 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

FILE LAST UPDATED: 09 APR 2002              <20020409/UP>
MOST RECENT DERWENT UPDATE            200222   <200222/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001.
    (EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION
    SEE HELP COST <<<

>>> FOR UP-TO-DATE INFORMATION ABOUT THE DERWENT CHEMISTRY
    RESOURCE, PLEASE VISIT
         http://www.derwent.com/chemistryresource/index.html <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

=> D QUE L103
```

```
L100          32 SEA FILE=WPIDS ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                 VECTOR#
L101       12635 SEA FILE=WPIDS ABB=ON  PLU=ON  IMMUNODEFICIENCY OR HIV
L102           7 SEA FILE=WPIDS ABB=ON  PLU=ON  L100 AND L101
L103           3 SEA FILE=WPIDS ABB=ON  PLU=ON  L102 NOT (PARVOVIRUS OR HAPTEN
                 OR SHUTTLE VECTOR OR EXONS)/TI


=> D QUE L105
L100          32 SEA FILE=WPIDS ABB=ON  PLU=ON  CONDITION? (5A) REPLICA? (5A)
                 VECTOR#
L104        1604 SEA FILE=WPIDS ABB=ON  PLU=ON  RIBOZYME
L105           2 SEA FILE=WPIDS ABB=ON  PLU=ON  L100 AND L104


=> S L103 OR L105
L111           3 L103 OR L105

=> FILE STNGUIDE
FILE 'STNGUIDE' ENTERED AT 14:44:26 ON 10 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr  5, 2002 (20020405/UP).

=> DUP REM L106 L109 L107 L110 L108 L111
FILE 'MEDLINE' ENTERED AT 14:47:14 ON 10 APR 2002

FILE 'BIOTECHNO' ENTERED AT 14:47:14 ON 10 APR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'EMBASE' ENTERED AT 14:47:14 ON 10 APR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

FILE 'BIOTECHDS' ENTERED AT 14:47:14 ON 10 APR 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD AND INSTITUTE FOR SCIENTIFIC INFORMATION

FILE 'HCAPLUS' ENTERED AT 14:47:14 ON 10 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 14:47:14 ON 10 APR 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD
PROCESSING COMPLETED FOR L106
PROCESSING COMPLETED FOR L109
PROCESSING COMPLETED FOR L107
PROCESSING COMPLETED FOR L110
PROCESSING COMPLETED FOR L108
PROCESSING COMPLETED FOR L111
L112          30 DUP REM L106 L109 L107 L110 L108 L111 (11 DUPLICATES REMOVED)

=> D IBIB AB CT 1-30

L112 ANSWER 1 OF 30  EMBASE  COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   2002064573  EMBASE
TITLE:              A system for small-molecule control of
                    conditionally replication-competent
```

adenoviral **vectors**.

AUTHOR: Chong H.; Ruchatz A.; Clackson T.; Rivera V.M.; Vile R.G.
CORPORATE SOURCE: R.G. Vile, Molecular Medicine Program, Mayo Clinic, Rochester, MN 55905, United States. vile.richard@mayo.edu

SOURCE: Molecular Therapy, (2002) 5/2 (195-203).
Refs: 39
ISSN: 1525-0016 CODEN: MTOHCK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Replication-competent adenoviral vectors are potentially far more efficient than replication-defective vectors. However, for reasons of safety, there is a need to restrict viral replication both spatially, by limiting replication to certain cell types, and temporally. To control replication temporally, we have developed a system, based on the small-molecule dimerizer rapamycin, for regulating the replication of adenoviral vectors. In this system, one adenoviral vector, AdC4, expresses transcription factors whose activity is regulated by the non-immunosuppressive rapamycin analog AP21967. A second vector, Ad(Z12-I-E1aE1b19k), contains E1 genes placed downstream of binding sites for the regulated transcription factor. Co-infection of several cell lines by the vector pair leads to dimerizer-dependent E1 expression and an increase in viral replication, as shown by Southern blots and replication assays. Furthermore, expression of a reporter gene from a replication-defective vector, Ad-GM-CSF, can be augmented by up to 18-fold by co-infection with the pair of **conditionally replicating vectors** in the presence of dimerizer.
Similar results are obtained when the vectors are directly injected into subcutaneous HT1080 xenograft tumors in nude mice. We believe that vectors based on this principle will be a useful additional tool to enhance efficiency and safety of gene delivery for anti-cancer therapy.

CT Medical Descriptors:
*adenovirus vector
*virus replication
molecular size
safety
cell type
gene expression
binding site
genetic regulation
virus infection
cell line
Southern blotting
assay
reporter gene
tumor xenograft
nude mouse
viral gene delivery system
sarcoma cell
human
nonhuman
mouse
animal experiment
animal model
controlled study
human cell

animal cell
article
Drug Descriptors:
rapamycin
transcription factor: EC, endogenous compound
rapamycin derivative
granulocyte macrophage colony stimulating factor
virus DNA: EC, endogenous compound

L112 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:544199 HCAPLUS
DOCUMENT NUMBER: 135:313299
TITLE: Comparative analyses of transgene delivery and expression in tumors inoculated with a **replication-conditional** or -defective **viral vector**
AUTHOR(S): Ichikawa, Tomotsogu; Chiocca, E. Antonio
CORPORATE SOURCE: Molecular Neuro-oncology Laboratory, Neurosurgery Service, Massachusetts General Hospital, Charlestown, MA, 02129, USA
SOURCE: Cancer Research (2001), 61(14), 5336-5339
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Viral vectors for cancer can be classified into those that do not replicate (replication-defective vectors) and those that selectively replicate in neoplastic cells (replication-conditional or oncolytic vectors). Both of these can deliver anticancer cDNAs for therapeutic purposes. Opposite hypotheses can be made regarding the advantages of each vector type with regard to anat. transgene expression. For the former vector, because cDNA delivery occurs in neoplastic cells that have the ability to migrate into the tumor mass, relatively extensive anat. and temporal expression of anticancer functions may occur. For the latter vector, active viral replication may permit anatomically and temporally extensive delivery of the foreign cDNA into the tumor mass. Herein, the authors performed a simple comparative anal. to test which of these hypotheses is valid. Direct inoculation of s.c. tumors with a replication-conditional or a replication-defective viral vector, each of which expressed lacZ cDNA, was performed. Tumors were excised and analyzed for anat. delivery of .beta.-galactosidase and for neoplastic viral titers. The authors find that lacZ cDNA expression is obsd. in approx. 40% of the tumor area 3, 7, and 14 days after injection with the replication-conditional vector, whereas approx. 10% of the tumor area expresses the transgene 3 days after injection with the replication-defective vector, with a rapid decline in expression thereafter. Titers of the replication-conditional virus remain stable within injected tumors for the 14 days of the assay (approx. 1:1,000 of the initial injection dose), whereas titers of the replication-defective vector decrease rapidly after injection (to a value of 1:100,000 of the initial injection dose). Taken in conjunction, these studies show that transgene delivery and expression in tumors last longer and are found throughout an anatomically more extensive area after injection with replication-conditional gene therapy vectors than after injection with replication-defective gene therapy vectors.
CT Antitumor agents
CT Gene therapy
CT Human herpesvirus 1
CT Transduction, genetic
CT Virus vectors

CT Transgene
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L112 ANSWER 3 OF 30 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2001:34075181 BIOTECHNO
TITLE: Human **immunodeficiency** virus type 1-mediated syncytium formation is compatible with adenovirus replication and facilitates efficient dispersion of viral gene products and De Novo-synthesized virus particles
AUTHOR: Li H.; Haviv Y.S.; Derdeyn C.A.; Lam J.; Coolidge C.; Hunter E.; Curiel D.T.; Blackwell J.L.
CORPORATE SOURCE: Dr. J.L. Blackwell, University of Alabama, WTI 620, 1824 6th Avenue South, Birmingham, AL 35294, United States.
E-mail: jerry.blackwell@ccc.uab.edu
SOURCE: Human Gene Therapy, (2001), 12/18 (2155-2165), 67 reference(s)
CODEN: HGTHE3 ISSN: 1043-0342
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Conditionally replicative** adenovirus (CRAd) **vectors** are designed for specific oncolytic replication in tumor tissues with concomitant sparing of normal cells. As such, CRAds offer an unprecedented level of anticancer potential for malignancies that have been refractory to previous cancer gene therapy interventions. CRAd efficacy may, however, be compromised by inefficient dispersion of the replicating vector within the tumor tissue. To address this issue, we evaluated the utility of a fusogenic membrane glycoprotein (FMG), which induces the fusion of neighboring cellular membranes to form multinucleated syncytia. We hypothesized that the FMG-mediated syncytia would facilitate dispersion of the adenovirus (Ad) gene products and viral progeny. To test this, human **immunodeficiency** virus type 1 (**HIV**-1) envelope glycoproteins, which induce syncytia in the presence of CD4.sup.+ target cells, were expressed by an Ad (Ad5HIVenv) in permissive (CD4-positive) and nonpermissive (CD4-negative) cell lines. After validating this Ad-FMG model, the efficiency of Ad replication in the presence or absence of syncytia was evaluated. The results demonstrated that syncytium formation was compatible with Ad replication and dramatically increased the dispersion of virus gene products within the cytoplasm of the syncytia as well as viral particles in the nuclei of the syncytial mass. Moreover, progeny virions were released more efficiently from syncytia compared with nonsyncytial cells. These data demonstrate the utility of FMGs as a dispersion agent and suggest that FMGs can improve the efficacy of CRAd gene therapy.
CT *Adenovirus; *virus replication; *gene product; syncytium; Human **immunodeficiency** virus 1; virus gene; virus particle; cell fusion; cell membrane; dispersion; protein expression; cell line; validation process; cytoplasm; cell secretion; virion; progeny; gene therapy; drug potentiation; human; controlled study; human cell; article; protein FMG; protein; envelope protein; CD4 antigen; glycoprotein; unclassified drug

L112 ANSWER 4 OF 30 MEDLINE
ACCESSION NUMBER: 2002092054 MEDLINE
DOCUMENT NUMBER: 21679195 PubMed ID: 11821940
TITLE: Long-term RNase P-mediated inhibition of HIV-1 replication

and pathogenesis.
AUTHOR: Hnatyszyn H; Spruill G; Young A; Seivright R; Kraus G
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami, FL, USA.
SOURCE: GENE THERAPY, (2001 Dec) 8 (24) 1863-71.
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020201
Last Updated on STN: 20020324
Entered Medline: 20020322

AB Advances in genetic analysis and a greater understanding of human immunodeficiency virus (HIV) molecular pathogenesis have identified critical viral targets for gene interference strategies. RNase P molecules have been proposed as a novel approach for gene targeting based upon their potent catalytic activity, as well as versatile external guide sequence (EGS) which can be modified to specifically recognize almost any target mRNA. We designed a truncated EGS to specifically recognize the highly conserved U5 region of HIV-1 mRNA and mediate subsequent cleavage of hybridized mRNA by the RNase P enzyme component. The active U5-EGS (560), as well as a disabled U5 EGS (560D) control, were cloned into plasmids containing proviral constructs and transfected into a CD4(+) T cell line that was thereafter infected with HIV-1 MN. CD4(+) T cells treated with the active U5 EGS (560) were observed to maintain CD4(+) expression and did not produce HIV p24 gag antigen, form syncytia or undergo apoptosis up to 30 days after infection. Identical cells expressing the inactivated form of the U5 RNase P EGS completely down-regulated CD4 expression, produced elevated levels of HIV-1, formed large syncytia and underwent apoptosis similar to untreated cells. HIV-1 replication and related cytopathology can be effectively inhibited in CD4(+) T cells expressing a protective U5 EGS (560).

CT Check Tags: Human
Annexin V: AN, analysis
Antigens, CD4: AN, analysis
*CD4-Positive T-Lymphocytes: IM, immunology
Cell Division
Cell Line
DNA, Viral: AN, analysis
*Endoribonucleases: GE, genetics
Flow Cytometry: MT, methods
*Gene Therapy: MT, methods
Genetic Vectors: AD, administration & dosage
***HIV Infections: TH, therapy**
HIV-1: GE, genetics
***HIV-1: PH, physiology**
***RNA, Catalytic: GE, genetics**
Retroviridae: GE, genetics
Transfection
*Virus Replication: GE, genetics

L112 ANSWER 5 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001324898 EMBASE
TITLE: A novel approach to cancer therapy using an oncolytic herpes virus to package amplicons containing cytokine genes.
AUTHOR: Carew J.F.; Kooby D.A.; Halterman M.W.; Kim S.-H.; Federoff H.J.; Fong Y.

CORPORATE SOURCE: Y. Fong, Department of Surgery, Memorial Sloan-Kettering Cancer Ctr., New York, NY 10021, United States. fongy@mskcc.org
SOURCE: Molecular Therapy, (2001) 4/3 (250-256).
Refs: 41
ISSN: 1525-0016 CODEN: MTOHCK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB There are two promising herpes viral-based anticancer strategies: one involves replication-defective viruses to transfer therapeutic transgenes, and the other involves replication-conditional oncolytic viruses, which selectively infect and destroy cancer cells directly. This study examines a novel dual herpesvirus preparation, which combines the immunostimulatory effects of amplicon-mediated IL2 expression with direct viral-induced oncolysis. The oncolytic virus G207 was used as the **helper virus** to package a herpes simplex virus (HSV)-amplicon vector carrying the gene IL2 (HSV-IL2), yielding a single preparation with two complementary modes of action. In vivo comparison was carried out in a syngeneic squamous cell carcinoma flank tumor model. We directly injected established tumors with HSV-IL2, G207, G207 mixed with HSV-IL2, or G207-packaged HSV-amplicon carrying the IL2 transgene (G207[IL2]). Significant inhibition of tumor growth was seen at 2 weeks in the G207[IL2]-treated tumors relative to controls (0.57 .+-. 0.44 cm(3) versus 39.45 .+-. 5.13 cm(3), P < 0.00001), HSV-IL2 (20.97 .+-. 4.60 cm(3)), and the G207 group (7.71 .+-. 2.10 cm(3)). This unique use of a replication-**conditional**, oncolytic virus to package a **replication**-incompetent amplicon **vector** demonstrates impressive efficacy in vitro and in vivo, and avoids the theoretical concerns of recombination with reversion to wild type.
CT Medical Descriptors:
*gene therapy
*Herpes simplex virus
*oncolytic virus
cancer chemotherapy
Herpes virus
DNA packaging
virus vector
virus replication
gene transfer
transgene
virus infectivity
cancer cell
immunostimulation
in vivo study
comparative study
squamous cell carcinoma: DT, drug therapy
tumor model
injection
cancer growth
in vitro study
theory
virus recombination

nonhuman
mouse
animal experiment
animal model
controlled study
animal cell
article
Drug Descriptors:
cytokine: EC, endogenous compound
interleukin 2: DT, drug therapy
interleukin 2: PR, pharmaceutics

L112 ANSWER 6 OF 30 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2000:30743988 BIOTECHNO
TITLE: Potent inhibition of human **immunodeficiency** virus type 1 replication by **conditionally replicating** human **immunodeficiency** virus-based lentiviral **vectors** expressing envelope antisense mRNA
AUTHOR: Mautino M.R.; Morgan R.A.
CORPORATE SOURCE: Dr. R.A. Morgan, Clinical Gene Therapy Branch, NHGRI, Building 10, 10 Center Drive, Bethesda, MD 20892-1851, United States.
E-mail: rmorgan@nhgri.nih.gov
SOURCE: Human Gene Therapy, (20 SEP 2000), 11/14 (2025-2037), 30 reference(s)
CODEN: HGTHE3 ISSN: 1043-0342
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We describe an **HIV**-based lentiviral vector that expresses a 1-kb antisense mRNA directed against the **HIV**-1 mRNAs containing env sequences. The expression of antisense env mRNAs (envAS) does not inhibit the synthesis of p24 expressed from the **HIV**-1 helper plasmid used to package the vector, as this helper has a deletion in the env gene. This allows the production of high-titer VSV-G pseudotyped lentiviral particles. In challenge experiments using unselected populations of SupT1 cells transduced with this vector, a complete inhibition of **HIV**-1 replication was observed for long periods of in vitro culture, even at high **HIV**-1 infectious doses. The potent inhibition of **HIV**-1 replication by this vector correlated with a low occurrence of mobilization of the vector to previously untransduced cells. The infectivity of the wild-type **HIV**-1 that escapes inhibition was highly inhibited, suggesting that the vector is providing **HIV**-1 inhibition of replication not only due to its antisense effect but also by competing for encapsidation and mobilization to noninfected cells.
CT *Human **immunodeficiency** virus infection; *virus inhibition; *expression vector; *complementary RNA; *messenger RNA; Lentivirinae; gene expression; protein synthesis inhibition; plasmid; gene deletion; virus particle; virus infectivity; virogenesis; human; nonhuman; human cell; article; antigen p24

L112 ANSWER 7 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000350574 EMBASE
TITLE: A novel, **conditionally replicative** adenovirus for the treatment of breast cancer that allows controlled replication of E1a-deleted adenoviral vectors.
AUTHOR: Hernandez-Alcoceba R.; Pihalja M.; Wicha M.S.; Clarke M.F.

CORPORATE SOURCE: M.F. Clarke, Dept. of Inte. Med.-Hematol./Oncol., Univ. Michigan Comprehen. Can. Ctr., 4-310 CCGC, 1500 E. Medical Ctr. Drive, Ann Arbor, MI 48109-0936, United States. mclarke@umich.edu

SOURCE: Human Gene Therapy, (20 Sep 2000) 11/14 (2009-2024). Refs: 42
ISSN: 1043-0342 CODEN: HGTHE3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
022 Human Genetics
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The efficiency of gene therapy strategies against cancer is limited by the poor distribution of the vectors in the malignant tissues. To solve this problem, a new generation of tumor-specific, conditionally replicative adenoviruses is being developed. To direct the replication of the virus to breast cancer, we have considered one characteristic present in a great proportion of these cancers, which is the expression of estrogen receptors (ERs). On the basis of the wild-type adenovirus type 5, we have constructed a conditionally replicative adenovirus (Ad5ERE2) in which the E1a and E4 promoters have been replaced by a portion of the pS2 promoter containing two estrogen-responsive elements (EREs). This promoter induces transcriptional activation of the E1A and E4 units in response to estrogens in cells that express the ERs. Ad5ERE2 is able to kill ER+ human breast cancer cell lines as efficiently as the wild-type virus, but has decreased capacity to affect ER- cells. By complementation of the E1a protein in trans, Ad5ERE2 allows restricted replication of a conventional E1a-deleted adenoviral vector. When a virus expressing the proapoptotic gene Bc1-xs (Clarke et al., Proc. Natl. Acad. Sci. U.S.A. 1995;92:11024-11028) is used in combination with Ad5ERE2, the ability of both viruses to induce cell death is dramatically increased, and the effect can be modulated by addition of the antiestrogen tamoxifen.

CT Medical Descriptors:
*breast cancer: ET, etiology
*gene therapy
*virus recombinant
*virus replication
Adenovirus
expression vector
promoter region
hormone responsive element
gene deletion
gene activation
apoptosis
genetic complementation
cytopathogenic effect
nude mouse
modulation
human
nonhuman
mouse
controlled study
human cell
adolescent
article
Drug Descriptors:

*estrogen receptor
estradiol
antiestrogen
tamoxifen

L112 ANSWER 8 OF 30 BIOTECHDS COPYRIGHT 2002 DERWENT INFO AND ISI
ACCESSION NUMBER: 2000-11743 BIOTECHDS
TITLE: Improved titers of **HIV**-based lenti virus vectors using the SRV-1 constitutive transport element; involving lenti virus vector-mediated gene transfer for expression in host cell
AUTHOR: Mautino M R; Keiser N; *Morgan R A
CORPORATE SOURCE: Nat.Cent.Hum.Genome-Res.Bethesda; Nat.Inst.Health-Bethesda
LOCATION: Clinical Gene Therapy Branch, NHGRI, 10 Center Drive, Building 10, Room 10C103, Bethesda, MD 20892-1851, USA.
SOURCE: Gene Ther.; (2000) 7, 16, 1421-24
CODEN: GETHEC
ISSN: 0969-7128
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The use of **HIV** virus-based **conditionally replicating vectors** expressing anti-**HIV** virus genes for the treatment of AIDS has several theoretical advantages. The development of lenti virus vectors that use Rev-independent mechanisms of nuclear export for their genomic RNA could facilitate the construction of novel anti-**HIV** virus vectors. The titers of Rev-independent lenti virus vectors having the SRV-1 constitutive transport element (CTE) were improved by mutating the major splice donor and acceptor sites present in the vector and by relocalization of the CTE sequences adjacent to the **HIV** virus-1 3' long terminal repeat. These two modifications have additive beneficial effects on vector titers and packaging efficiency. Packaging these CTE+ vectors expressing marker genes with a Rev-dependent **HIV** virus-1 helper vector yields higher titers than were obtained using a Rev-dependent lenti virus vector. A lenti virus vector whose genomic mRNA did not require Rev for transport to the cytoplasm would possess a competitive advantage for packaging. (17 ref)
CT **HIV** VIRUS-BASED REV-INDEPENDENT LENTI VIRUS VECTOR-MEDIATED GENE TRANSFER, EXPRESSION IN HOST CELL, CONSTITUTIVE TRANSPORT ELEMENT, APPL. **HIV**-VIRUS INFECTION GENE THERAPY LEUKO VIRUS RETRO VIRUS LENTI VIRUS AIDS (VOL.19, NO.20)

L112 ANSWER 9 OF 30 BIOTECHDS COPYRIGHT 2002 DERWENT INFO AND ISI
ACCESSION NUMBER: 1999-07571 BIOTECHDS
TITLE: Expressing a gene from **conditionally replicating** viral **vector**; modified non-pathogenic **HIV** virus vector containing **ribozyme** or antisense oligonucleotide, has virucide activity and competes with wild-type **HIV** virus, useful for **HIV** virus infection therapy
AUTHOR: Dropulic B; Pitha P M
PATENT ASSIGNEE: Univ.Johns-Hopkins
LOCATION: Baltimore, MD, USA.
PATENT INFO: US 5888767 30 Mar 1999
APPLICATION INFO: US 1997-917625 22 Aug 1997
PRIORITY INFO: US 1997-917625 22 Aug 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1999-243205 [20]

AB A method of expressing a gene from a **conditionally replicating vector** is new and comprises transfecting a host cell with a **conditionally replicating HIV** virus **vector** (I) and a wild-type strain of **HIV**, a helper virus or a helper vector. (I) contains at least one other nucleic acid sequence (II) and replicates in the host cell only when complemented by (II) which causes the preferential packaging of (I) into progeny virions over wild-type virions. (I) establishes a competitive, but non-pathogenic, infection. (I) inherently target cells infected with the **HIV** virus, particularly the microglia of the brain which are normally difficult to target. (I) is unlikely to be toxic to uninfected cells as it produces no viral proteins and following its systematic spread, reduces the **HIV** virus load of the blood. (II) is a genetic virucide agent that adversely affects wild-type **HIV** virus but not (I). It is especially an antisense oligonucleotide or a **ribozyme**, particularly one that cuts the nucleotide motif, NUH. (I) may also include a multidrug-resistance gene to give it a selective advantage. (31pp)

CT **HIV** VIRUS VECTOR-MEDIATED **RIBOZYME**, ANTISENSE OLIGONUCLEOTIDE VIRUCIDE EXPRESSION IN TARGET CELL, APPL. INFECTION GENE THERAPY RNA ENZYME LEUKO VIRUS RETRO VIRUS AIDS (VOL.18, NO.13)

L112 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 1999:205258 HCAPLUS
DOCUMENT NUMBER: 130:233260
TITLE: **Conditionally replicating viral vectors** and their use in vaccines, **viral** infection treatment, or cancer therapy
INVENTOR(S): Dropulic, Boro; Pitha, Paula M.
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: U.S., 31 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5885806	A	19990323	US 1996-758598	19961127
US 5888767	A	19990330	US 1997-917625	19970822
US 6114141	A	20000905	US 1999-251085	19990216
US 6207426	B1	20010327	US 1999-251084	19990216
US 6232120	B1	20010515	US 1999-251283	19990216
US 6168953	B1	20010102	US 1999-312322	19990514

PRIORITY APPLN. INFO.:
US 1995-32800P P 19951128
US 1996-758598 A3 19961127
US 1997-917625 A3 19970822
US 1999-251283 A3 19990216

AB The present invention provides a **conditionally replicating** viral vector, methods of making, modifying, propagating and selectively packaging, and using such a vector, isolated mols. of specified nucleotide and amino acid sequences relevant to such vectors, a pharmaceutical compn. and a host cell comprising such a vector, and the use of such a host cell to screen drugs. The methods include the prophylactic and therapeutic treatment of viral infection, in particular HIV infection, and, thus, are also directed to viral vaccines and the treatment of cancer, in particular cancer of viral etiol. Other methods include the use of such **conditionally replicating**

viral vectors in gene therapy and other applications. Examples include **conditionally replicating** HIV vectors crHIV-1.1, crHIV-1.11, crHIV-1.12, and crHIV-1.111. Examples also include use of triple anti-TAT ribozyme cassettes to cleave HIV nucleic acids.

CT LTR (long terminal repeat)
CT tat gene (microbial)
CT Human immunodeficiency virus 1
CT Antitumor agents
CT **Antiviral agents**
CT DNA sequences
CT Drug screening
CT Gene therapy
CT Synthetic vaccines
CT **Antisense oligonucleotides**
CT **Ribozymes**
CT **Retroviral vectors**
CT **Retroviral vectors**
CT **Retroviral vectors**
CT **Retroviral vectors**
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L112 ANSWER 11 OF 30 BIOTECHDS COPYRIGHT 2002 DERWENT INFO AND ISI
ACCESSION NUMBER: 1999-07567 BIOTECHDS
TITLE: New **conditionally replicating** viral **vector**;
expression in host cell, used for drug screening and infection gene therapy
AUTHOR: Dropulic B; Pitha P M
PATENT ASSIGNEE: Univ.Johns-Hopkins
LOCATION: Baltimore, MD, USA.
PATENT INFO: US 5885806 23 Mar 1999
APPLICATION INFO: US 1996-758598 27 Nov 1996
PRIORITY INFO: US 1996-758598 27 Nov 1996
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1999-228537 [19]

AB A **conditionally replicating HIV** virus **vector**, is new. Also claimed are: a method of producing the vector which involves obtaining a wild-type **HIV** virus-derived starting vector with host cell-specific replication, and incorporating a nucleic acid sequence that comprises or encodes a genetic virucide into the vector, and producing a product vector which is selectively packaged into progeny virions over a wild-type strain of **HIV** virus sensitive to the genetic antiviral agent, or a helper virus/vector sensitive to the genetic virucide; a **conditionally replicating HIV** virus **vector**; a method of modifying a vector which involves obtaining a DNA **HIV** virus vector and introducing a specified DNA sequence; and an RNA nucleotide containing the DNA sequence. The **conditionally replicating vector** may be used to produce a treatment against a wide range of virus infections. Also disclosed are host cells containing the vector, the use of the host ell for drug screening, and the use of the vector for gene therapy. (31pp)

CT **CONDITIONALLY REPLICATING HIV** VIRUS **VECTOR** CONSTRUCTION, EXPRESSION IN HOST CELL, APPL. DRUG SCREENING, INFECTION GENE THERAPY LEUKO VIRUS RETRO VIRUS AIDS (VOL.18, NO.13)

L112 ANSWER 12 OF 30 MEDLINE

ACCESSION NUMBER: 2001668334 MEDLINE
DOCUMENT NUMBER: 21570756 PubMed ID: 11713796
TITLE: The application of ribozymes to HIV infection.
AUTHOR: Rossi J J
CORPORATE SOURCE: Department of Molecular Biology, Graduate School of Biological Sciences, Beckman Research Institute of the City of Hope, Duarte, CA 91010, USA.. jrossi@coh.org
SOURCE: Curr Opin Mol Ther, (1999 Jun) 1 (3) 316-22. Ref: 66
Journal code: 100891485. ISSN: 1464-8431.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011121
Last Updated on STN: 20020124
Entered Medline: 20011231

AB During the past decade major advances have been made in combating HIV infection and reducing the incidence of AIDS in the western world. Despite optimism about such progress, there is accumulating evidence to suggest that new forms of therapy may be necessary to combat viral resistance to current drugs as well as to provide alternatives to life-long drug use. Genetic forms of therapy are considered to be an important alternative to current drug therapy. One therapeutic agent that can be tailored to inhibit viral infection is catalytic RNA or ribozymes. These RNAs can be engineered to site-specifically cleave targeted RNAs, thereby minimizing cellular toxicity associated with conventional drugs. A potential advantage of ribozymes over other forms of genetic therapy aside from target specificity is their potential for interfering with different stages of the viral life cycle. Ribozymes can be designed and expressed to interfere with viral entry, messenger RNA function and viral packaging. For the two simplest ribozyme motifs, the hammerhead and hairpin, there are hundreds of potential sites along the viral genome. Combinatorial use of ribozymes allows multiple HIV-1 sequences to be attacked simultaneously, thereby circumventing viral resistance through mutation. Ribozymes can also be designed to inhibit expression of cellular targets, which are required for HIV-1 infection. The successful applications of ribozymes against HIV-1 in preclinical settings has now set the stage for their testing in patient trials and several first phase clinical trials are currently underway.

CT Check Tags: Animal; Human
Anti-HIV Agents: CH, chemistry
***Anti-HIV Agents: TU, therapeutic use**
Clinical Trials, Phase I
Clinical Trials, Phase II
Cohort Studies
Combinatorial Chemistry Techniques
Drug Design
Drug Evaluation, Preclinical
*Gene Therapy
Genetic Vectors: GE, genetics
Genetic Vectors: TU, therapeutic use
***HIV Infections: DT, drug therapy**
***HIV-1: GE, genetics**
HIV-1: PH, physiology
Mice
Nucleic Acid Conformation
RNA: AI, antagonists & inhibitors

RNA: GE, genetics
RNA, Catalytic: CH, chemistry
***RNA, Catalytic: TU, therapeutic use**
RNA, Messenger: AI, antagonists & inhibitors
RNA, Messenger: GE, genetics
RNA, Transfer, Lys: AI, antagonists & inhibitors
RNA, Transfer, Lys: GE, genetics
*RNA, Viral: AI, antagonists & inhibitors
RNA, Viral: GE, genetics
Receptors, CCR5: GE, genetics
Tumor Viruses, Murine: GE, genetics

L112 ANSWER 13 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999052662 EMBASE
TITLE: New cloning vectors with temperature-sensitive replication.
AUTHOR: Phillips G.J.
CORPORATE SOURCE: G.J. Phillips, Department of Microbiology, Iowa State University, Ames, IA 50011, United States. gregory@iastate.edu
SOURCE: Plasmid, (1999) 41/1 (78-81).
Refs: 35
ISSN: 0147-619X CODEN: PLSMDX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A series of cloning vectors with conditional, temperature-sensitive replication that are selectable with ampicillin, chloramphenicol, and kanamycin has been constructed. These vectors are derivatives of a pSC101 mutant that can replicate only at low temperatures. The cloning vectors carry a number of unique restriction sites and provide for screening of recombinant plasmids by a complementation. These vectors have proven useful for a variety of applications where **conditional replication** of a recombinant plasmid is desired.
CT Medical Descriptors:
***cloning vector**
*temperature sensitive mutant
DNA replication
escherichia coli
salmonella
recombinant plasmid
nonhuman
article
Drug Descriptors:
bacterial DNA: EC, endogenous compound

L112 ANSWER 14 OF 30 MEDLINE
ACCESSION NUMBER: 1998312633 MEDLINE
DOCUMENT NUMBER: 98312633 PubMed ID: 9650613
TITLE: Preclinical characterization of an anti-tat ribozyme for therapeutic application.
AUTHOR: Wang L; Witherington C; King A; Gerlach W L; Carr A; Penny R; Cooper D; Symonds G; Sun L Q
CORPORATE SOURCE: Johnson and Johnson Research Laboratories, Sydney, NSW, Australia.
SOURCE: HUMAN GENE THERAPY, (1998 Jun 10) 9 (9) 1283-91.
Journal code: A12; 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980916

AB A hammerhead ribozyme retroviral construct, denoted RRz2, targeting the coding region of the human immunodeficiency virus type 1 (HIV-1) tat gene, has shown itself to be effective in a range of test systems. Inhibition of the replication of HIV-1 IIIB and primary drug-resistant strains in pooled transduced CEMT4 cells was consistently found to be more than 80% compared with the control-vector transduced cells, whereas a mutant RRz2 gave approximately 45% inhibition. A multiple HIV-1 passage assay showed the absence of emergence of mutations within the specific viral RNA ribozyme target sequences. This lack of generation of ribozyme "escape mutants" occurred despite the almost complete disappearance of a HIV-1 quasi-species in the testing virus. When RRz2 was tested in peripheral blood lymphocytes (PBLs) from HIV-1-infected patients, paired analysis showed that cell viability in the ribozyme-transduced HIV-1-infected PBLs was significantly higher than that in the vector-transduced cells. This difference in viability (vector versus RRz2) was not observed in PBLs from non-HIV-1-infected donors. Taken together, these results indicate that the transfer of an anti-HIV-1 ribozyme gene into human T lymphocytes could have major impact on viral replication and T cell viability in the HIV-1-infected individual.

CT Check Tags: Human; Support, Non-U.S. Gov't
Base Sequence
Cell Line
DNA, Viral: AN, analysis
*Gene Therapy: MT, methods
*Genes, tat: GE, genetics
Genetic Vectors
HIV Infections: VI, virology
***HIV-1: GE, genetics**
***HIV-1: ME, metabolism**
Leukocytes, Mononuclear: VI, virology
Molecular Sequence Data
RNA, Antisense: AN, analysis
***RNA, Catalytic: ME, metabolism**
RNA, Viral: AN, analysis
Retroviridae
T-Lymphocytes: VI, virology
Transcription, Genetic
Transduction, Genetic
Virus Replication

L112 ANSWER 15 OF 30 BIOTECHDS COPYRIGHT 2002 DERWENT INFO AND ISI
ACCESSION NUMBER: 1997-09060 BIOTECHDS
TITLE: **Conditionally replicating** viral **vectors** including DNA that imparts selective advantage;
HIV virus or toga virus vector for use in virus infection or cancer gene therapy, intracellular immunization or nucleic acid vaccine strategies
AUTHOR: Dropulic B; Pitha P M
PATENT ASSIGNEE: Univ.Johns-Hopkins
LOCATION: Baltimore, MD, USA.
PATENT INFO: WO 9720060 5 Jun 1997
APPLICATION INFO: WO 1996-US18997 27 Nov 1996
PRIORITY INFO: US 1997-563459 28 Nov 1997

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1997-319459 [29]
AB A new **conditionally replicating** virus **vector** **replicates** only in a permissive host cell, and contains a sequence conferring a selective advantage over a corresponding wild-type or helper virus strain. The vector may contain a sequence encoding a virucidal agent, adversely affecting replication and/or expression of another virus, e.g. an antisense, **ribozyme** or immunogen gene (nucleic acid vaccine). The vector is preferably derived from **HIV** virus or a toga virus. The vector preferably lacks the **HIV** tat gene and its splice site, and contains a triple anti-Tat **ribozyme** DNA cassette, with catalytic domains cleaving different sites in wild-type **HIV**, and optionally mutant protease and/or mutant reverse-transcriptase (EC-2.7.7.49) sequences. The vector is preferably crHIV-1.1, crHIV-1.11, crHIV-1.12 or crHIV-1.111. A packaging cell culture producing the vector is also new. The vector may be used along with a cytostatic agent, protease-inhibitor and/or reverse-transcriptase-inhibitor to treat virus infection or cancer via gene therapy or intracellular immunization, etc. (114pp)
CT CONDITIONALLY REPLICATING **HIV** VIRUS, TOGA VIRUS VECTOR, ANTISENSE, ANTI-TAT **RIBOZYME**, IMMUNOGEN NUCLEIC ACID VACCINE GENE TRANSFER, EXPRESSION, APPL. VIRUS INFECTION, CANCER GENE THERAPY, INTRACELLULAR IMMUNIZATION, ETC. LEUKO VIRUS RETRO VIRUS RNA ENZYME TUMOR HUMAN MAMMAL ANIMAL PROTEASE REVERSE-TRANSCRIPTASE EC-2.7.7.49 CRHIV-1.1 CRHIV-1.11 CRHIV-1.12 CRHIV-1.111 PACKAGING CELL CULTURE DNA CASSETTE DNA SEQUENCE (VOL.16, NO.17)

L112 ANSWER 16 OF 30 MEDLINE
ACCESSION NUMBER: 97479364 MEDLINE
DOCUMENT NUMBER: 97479364 PubMed ID: 9338016
TITLE: Inhibition of HIV-1 replication by retroviral vectors expressing monomeric and multimeric hammerhead ribozymes.
AUTHOR: Ramezani A; Ding S F; Joshi S
CORPORATE SOURCE: Department of Medical Genetics and Microbiology, Faculty of Medicine, University of Toronto, Ontario, Canada.
SOURCE: GENE THERAPY, (1997 Aug) 4 (8) 861-7.
Journal code: CCE; 9421525. ISSN: 0969-7128.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971119
AB Retroviral vectors were engineered to express monomeric and multimeric hammerhead ribozymes targeting one and nine highly conserved sites within the HIV-1 envelope (Env) coding region. In vitro, both the monomeric and multimeric ribozymes were shown to be active and cleave the target RNA containing the cleavage sites. A human CD4+ T lymphocyte-derived MT4 cell line was stably transduced with retroviral vectors expressing these ribozymes. Ribozyme expression in stably transduced cells was confirmed by Northern blot analysis and reverse-transcription polymerase chain reaction (RT-PCR). As compared with the control cells lacking any ribozyme, HIV-1 replication was delayed in monomeric RzEnv-expressing cells. Virus replication was almost completely inhibited in multimeric RzEnv1-9-expressing cells as no viral RNA or protein could be detected in these cells and in their culture supernatants for up to 60 days after infection. The genomic DNA from RzEnv1-9-expressing cells was shown to

contain HIV-1 proviral DNA sequences at days 3 and 60 after HIV infection. HIV-1 used in the challenge experiments was found to contain fully reverse transcribed '-' strand DNA which should have been able to infect complete proviral DNA synthesis and integrate within the cellular genome without being affected by pre-existing ribozymes. Therefore, the proviral DNA present at day 3 after infection may have originated from infection by such DNA-containing virus particles. The results obtained with the retroviral vector expressing RzEnv1-9 are very encouraging and we envisage its future use in anti-HIV-1 gene therapy.

CT Check Tags: Human; Support, Non-U.S. Gov't
CD4-Positive T-Lymphocytes: VI, virology
Cells, Cultured
*DNA Replication
DNA, Viral: AN, analysis
*Gene Therapy: MT, methods
***Genetic Vectors**
HIV-1: GE, genetics
***HIV-1: PH, physiology**
RNA, Catalytic
RNA, Viral: AN, analysis
***Retroviridae**
*Virus Replication

L112 ANSWER 17 OF 30 MEDLINE
ACCESSION NUMBER: 97316827 MEDLINE
DOCUMENT NUMBER: 97316827 PubMed ID: 9174101
TITLE: Use of adenoviral VAI small RNA as a carrier for cytoplasmic delivery of ribozymes.
AUTHOR: Prislei S; Buonomo S B; Michienzi A; Bozzoni I
CORPORATE SOURCE: Istituto Pasteur, Fondazione Cenci-Bolognetti, Dipartimento di Genetica e Biologia Molecolare, Universita La Sapienza, Roma, Italy.
SOURCE: RNA, (1997 Jun) 3 (6) 677-87.
Journal code: CHB; 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970709
Last Updated on STN: 19970709
Entered Medline: 19970624

AB The in vivo effectiveness of therapeutic RNAs, like antisense molecules and ribozymes, relies on several features: RNA molecules need to be expressed at high levels in the correct cellular compartment as stable and active molecules. The exploitation of "natural" small RNA coding genes as expressing cassettes gives high chances to fulfill these requirements. We have investigated the utilization of the adenoviral VAI RNA as a cytoplasmatic carrier for expressing ribozymes against HIV-1. The conserved 5' leader sequence of HIV was chosen as a target, because it is present in all the viral transcripts and is highly conserved. Hammerhead ribozymes were substituted to different portions of the VAI RNA and the resulting chimera were tested in the in vivo system of Xenopus laevis oocytes for their level of accumulation, cellular compartmentalization, association with specific ribonucleoparticles containing the La antigen. Significant differences in the activity of the different chimera were revealed by in vitro cleavage assays and S100 extracts of injected oocytes. The catalytic activity of the ribozymes in the RNP context

mal; Support, Non-U.S. Gov't

Searched by Thom Larson, STIC, 308-7309

*Adenoviruses, Human: GE, genetics
Anti-HIV Agents: PD, pharmacology
Autoantigens: ME, metabolism
Cell Compartmentation
Cytoplasm: ME, metabolism
Gene Transfer Techniques
***Genetic Vectors**
HIV-1: DE, drug effects
Microinjections
Oocytes
***RNA, Catalytic: GE, genetics**
RNA, Catalytic: PD, pharmacology
*RNA, Viral: GE, genetics
Ribonucleoproteins: ME, metabolism
Transcription, Genetic
Xenopus laevis

L112 ANSWER 18 OF 30 MEDLINE
ACCESSION NUMBER: 97348450 MEDLINE
DOCUMENT NUMBER: 97348450 PubMed ID: 9204460
TITLE: Retroviral delivery and anti-HIV testing of hammerhead ribozymes.
AUTHOR: Cagnon L; Rossi J
CORPORATE SOURCE: Department of Molecular Biology, Beckman Research Institute of the City of Hope, Duarte, CA, USA.
CONTRACT NUMBER: AI 25959 (NIAID)
AI 29329 (NIAID)
SOURCE: METHODS IN MOLECULAR BIOLOGY, (1997) 74 451-7.
Journal code: BU3; 9214969. ISSN: 1064-3745.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970908
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
***Anti-HIV Agents: AD, administration & dosage**
***Anti-HIV Agents: PD, pharmacology**
Cell Line
Drug Delivery Systems
Gene Expression
Gene Therapy
Genetic Vectors
HIV Core Protein p24: AN, analysis
HIV Infections: TH, therapy
HIV-1: DE, drug effects
HIV-1: GE, genetics
***RNA, Catalytic: AD, administration & dosage**
RNA, Catalytic: GE, genetics
***RNA, Catalytic: PD, pharmacology**
***Retroviridae: GE, genetics**
T-Lymphocytes: VI, virology
Transduction, Genetic
Transfection

L112 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:434836 HCAPLUS
DOCUMENT NUMBER: 127:144582

TITLE: **Conditionally replicative** adenoviruses for cancer therapy
AUTHOR(S): Rancourt, Claudine; Curiel, David T.
CORPORATE SOURCE: Gene Therapy Program, University of Alabama at Birmingham, 1824 6th Avenue, South, Room 620 Wallace Tumor Institute, Birmingham, USA
SOURCE: Adv. Drug Delivery Rev. (1997), 27(1), 67-81
CODEN: ADDREP; ISSN: 0169-409X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 104 refs. The delineation of the genetic etiol. of cancer makes gene therapy a rational approach for the mol. treatment of cancer. Many gene delivery systems have been developed, with viral vectors being the most effective. Underlying cancer gene therapy protocols is the recognition that quant. tumor transduction cannot be achieved with the vector systems available at the present time. One way to overcome this problem could be to amplify the transduction efficiency through the use of vectors capable of replicating specifically in tumor cells. We are currently developing an adenoviral vector in which viral replication will be restricted to the target tumor cells by limiting the expression of viral genes essential for the virus replication only to the tumor cells of interest.

CT **Retroviral vectors**
CT Adenoviridae
CT Antitumor agents
CT Gene therapy

L112 ANSWER 20 OF 30 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97008140 MEDLINE
DOCUMENT NUMBER: 97008140 PubMed ID: 8855316
TITLE: A **conditionally replicating** HIV-1 **vector** interferes with wild-type HIV-1 replication and spread.
AUTHOR: Dropulic B; Hermankova M; Pitha P M
CORPORATE SOURCE: Oncology Center, Johns Hopkins University School of Medicine, Baltimore, MD 21231, USA.. dropulic@welchlink.welch.jhu.edu
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Oct 1) 93 (20) 11103-8.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961125

AB Defective-interfering viruses are known to modulate virus pathogenicity. We describe **conditionally replicating** HIV-1 (crHIV) **vectors** that interfere with wild-type HIV-1 (wt-HIV) replication and spread. crHIV vectors are defective-interfering HIV genomes that do not encode viral proteins and replicate only in the presence of wt-HIV helper virus. In cells that contain both wt-HIV and crHIV genomes, the latter are shown to have a selective advantage for packaging into progeny virions because they contain ribozymes that cleave wt-HIV RNA but not crHIV RNA. A crHIV vector containing a triple anti-U5 ribozyme significantly interferes with wt-HIV replication and spread. crHIV vectors are also shown to undergo the full viral replicative cycle after

complementation with wt-HIV helper-virus. The application of defective interfering crHIV vectors may result in competition with wt-HIVs and decrease pathogenic viral loads in vivo.

CT Check Tags: Human; Support, Non-U.S. Gov't
Cell Line
Defective Viruses
***Genetic Vectors**
*HIV-1: GE, genetics
RNA, Catalytic: ME, metabolism
RNA, Viral: ME, metabolism
***Viral Interference**
Virion: ME, metabolism
*Virus Replication

L112 ANSWER 21 OF 30 MEDLINE
ACCESSION NUMBER: 96415740 MEDLINE
DOCUMENT NUMBER: 96415740 PubMed ID: 8818647
TITLE: Ex vivo transduction and expansion of CD4+ lymphocytes from HIV + donors: prelude to a ribozyme gene therapy trial.
AUTHOR: Leavitt M C; Yu M; Wong-Staal F; Looney D J
CORPORATE SOURCE: Department of Medicine and Biology, University of California San Diego, USA.
CONTRACT NUMBER: P30 AI36214-02 (NIAID)
U19 AI36612-01 (NIAID)
SOURCE: GENE THERAPY, (1996 Jul) 3 (7) 599-606.
Journal code: CCE; 9421525. ISSN: 0969-7128.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19980206
Entered Medline: 19961203

AB Preparations for a phase I trial of ex vivo, anti-HIV ribozyme gene therapy have included optimization of transduction and expansion of CD4+ lymphocytes from HIV-1 infected donors, using reagents suitable for production of cell products for human infusion. We also determined whether transduction by the ribozyme vector would inhibit replication and spread of endogenous HIV-1, and result in preferential survival of ribozyme-transduced CD4+ cells during lymphocyte expansion. Transduction efficiency, as estimated by DNA quantitative competitive (QC)-PCR, was similar for both control (LNL6) and ribozyme expressing (MJT) murine retroviral vectors (approximately 20%.) In the absence of antiviral agents, cells transduced with MJT exhibited three-fold greater numbers of CD4+ cells 2 weeks after transduction than did LNL6 transduced cells. In addition, viral replication was delayed 2-3 weeks in MJT transduced cultures. Both transduced cell populations expanded by 2-3 logs within 2 weeks. The clinical protocol involves infusion of both ribozyme and control vector transduced cells, making identification of agents capable of suppressing replication and spread of endogenous virus during ex vivo expansion necessary. The combination of nevirapine (100 nM) and CD4-PE40 (100 nM) completely suppressed endogenous virus replication in cultures transduced with either vector. At reduced concentrations of nevirapine, virus replication was suppressed only in MJT transduced cells.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Anti-HIV Agents: TU, therapeutic use
CD4-Positive T-Lymphocytes: CY, cytology
*CD4-Positive T-Lymphocytes: ME, metabolism

CD8-Positive T-Lymphocytes: CY, cytology
Cell Survival
Cells, Cultured
Clinical Trials, Phase I
Gene Therapy
***Genetic Vectors**
HIV Core Protein p24: ME, metabolism
HIV Seropositivity: BL, blood
***HIV Seropositivity: TH, therapy**
***HIV-1: DE, drug effects**
Leukocytes, Mononuclear: CY, cytology
Mice
Nevirapine
Pyridines: TU, therapeutic use
***RNA, Catalytic: GE, genetics**
***Retroviridae: GE, genetics**
*Transfection

L112 ANSWER 22 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96068787 EMBASE
DOCUMENT NUMBER: 1996068787
TITLE: **Conditionally replicative** and conjugative plasmids carrying lacZ.alpha. for cloning, mutagenesis, and allele replacement in bacteria.
AUTHOR: Metcalf W.W.; Jiang W.; Daniels L.L.; Kim S.-K.; Haldimann A.; Wanner B.L.
CORPORATE SOURCE: Department of Biological Sciences, Purdue University,West Lafayette, IN 47907, United States
SOURCE: Plasmid, (1996) 35/1 (1-13).
ISSN: 0147-619X CODEN: PLSMDX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We describe several new cloning vectors for mutagenesis and allele replacement experiments. These plasmids have the R6K.gamma. DNA replication origin (oriR(R6K.gamma.)) so they replicate only in bacteria supplying the .PI. replication protein (encoded by pir), and they can be maintained at low or high plasmid copy number by using Escherichia coli strains encoding either wild-type or mutant forms of .PI.. They also carry the RP4 transfer origin (oriT(RP4)) so they can be transferred by conjugation to a broad range of bacteria. Most of them encode lacZ.alpha. for blue-white color screening of colonies for ones with plasmids carrying inserts, as well as the f1 DNA replication origin for preparation of single stranded DNA. Particular plasmids are especially useful for allele replacement experiments because they also encode a positive counterselectable marker. One set carries tetAR (from Tn/0) that allows for positive selection of plasmid-free segregants as tetracycline-sensitive (Tet(S)) recombinants. Another set carries sacB (from Bacillus subtilis) that allows selecting plasmid-free segregants as sucrose-resistant (Suc(R)) ones. Accordingly, derivatives of these plasmids can be introduced into a non-pir host (via conjugative transfer, transformation, or electroporation), and integrants with the plasmid recombined into the chromosome via homologous sequences are selected using a plasmid antibiotic resistance marker. Plasmid- free segregants with an allele replacement can be subsequently selected as Tet(S) or Suc(R) recombinants. A number of additional features (including the presence of multiple cloning sites flanked by T3 and T7 RNA polymerase promoters) make these plasmids useful as general cloning vectors as well.

CT Medical Descriptors:
*allele
*bacterium conjugation
*molecular cloning
article
bacillus subtilis
bacterium mutant
cloning vector
dna replication
escherichia coli
nonhuman
plasmid

L112 ANSWER 23 OF 30 MEDLINE
ACCESSION NUMBER: 96002913 MEDLINE
DOCUMENT NUMBER: 96002913 PubMed ID: 7584112
TITLE: Inhibition of HIV-1 in CEM cells by a potent TAR decoy.
AUTHOR: Lee S W; Gallardo H F; Gaspar O; Smith C; Gilboa E
CORPORATE SOURCE: Program of Molecular Biology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.
CONTRACT NUMBER: 5 R37 AI28771 (NIAID)
K08 A10-121-01A1
SOURCE: GENE THERAPY, (1995 Aug) 2 (6) 377-84.
Journal code: CCE; 9421525. ISSN: 0969-7128.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951204

AB TAR decoys are short RNA oligonucleotides, corresponding to the HIV TAR sequence, which inhibit HIV expression and replication by blocking the binding of the HIV regulatory protein Tat to the authentic TAR region. In previous studies, TAR decoys expressed from a tRNA polIII promoter were moderately effective at inhibiting HIV in isolated human T cell lines and less effective at inhibiting HIV in peripheral blood CD4+ T cells. In this study, a series of modifications was introduced into the tRNA expression cassette in order to improve their effectiveness. These modifications included the addition of sequences which are predicted to have stem-loop secondary structures and addition of a wild-type tRNA processing site. TAR decoy RNA expressed in CEM cells from modified tRNA-based expression cassettes yielded five- to 20-fold more TAR transcripts than unmodified tRNA-based expression cassettes. HIV replication, as measured by a flow cytometric method to quantify intracellular viral p24 expression, was significantly reduced in polyclonal populations of CEM cells expressing a modified tRNA-TAR transcript that contains a wild-type tRNA processing site and stem-loops 5' and 3' to the TAR sequence. Similar modifications to the tRNA expression cassette also increased the intracellular concentration of a random test oligonucleotide, indicating that this improved expression system may also be useful for antisense and ribozyme based gene inhibition strategies.

CT Check Tags: Comparative Study; Human; Support, U.S. Gov't, P.H.S.
***Antiviral Agents: PD, pharmacology**
Sequence
ive T-Lymphocytes: IM, immunology
T-Lymphocytes: VI, virology

ured

Searched by Thom Larson, STIC, 308-7309

Gene Expression
*Gene Products, tat: ME, metabolism
***Genetic Vectors**
HIV Core Protein p24: AN, analysis
HIV Core Protein p24: BI, biosynthesis
HIV-1: DE, drug effects
HIV-1: GE, genetics
***HIV-1: PH, physiology**
Molecular Sequence Data
Moloney Leukemia Virus: GE, genetics
Nucleic Acid Conformation
Oligodeoxyribonucleotides
Oligoribonucleotides: ME, metabolism
*Oligoribonucleotides: PD, pharmacology
Promoter Regions (Genetics)
RNA, Catalytic: ME, metabolism
*RNA, Transfer: BI, biosynthesis
RNA, Transfer: CH, chemistry
*Regulatory Sequences, Nucleic Acid
T-Lymphocytes: IM, immunology
*T-Lymphocytes: VI, virology
Transcription, Genetic
*Transfection
Tumor Cells, Cultured
*Virus Replication: DE, drug effects

L112 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:570527 HCAPLUS
DOCUMENT NUMBER: 121:170527
TITLE: Mutants of HIV for suppression of HIV infection
INVENTOR(S): Alwine, James C.; Gonzalez-Scarano, Francisco; Zeichner, Steven L.; Malim, Michael H.
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA; Children's Hospital of Philadelphia
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9416060	A1	19940721	WO 1994-US377	19940111

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1993-2609 19930111
AB A human immunodeficiency virus (HIV) contg. a mutation on the long terminal repeat (LTR) sequence, which renders the virus **conditionally replication** incompetent in the absence of wild-type Tat protein supplied in trans, is provided to suppress the viral replication in the HIV-infected patients. Replication-incompetent HIV strains -147/-130 NXS, -165/148 NXS, and -201/-284 NXS are prepd. A transdominant gene such as Rev may be further mutagenized to suppress the reversion of replication. Addnl. gene encoding a cytotoxic agent such as Ricin A subunit may be incorporated into the virus to kill the HIV-infected cells. Human patients can be treated by introducing the myeloid cells or blood cells infected with the HIV mutants.
CT Monocyte
CT Bone marrow

CT **Ribozymes**
CT Ricins
CT Lymphocyte
CT **Ribonucleic acids**
CT Gene, microbial
CT Virus, animal
CT Genetic element
CT Gene, microbial
CT Gene, microbial
CT Gene, microbial
CT Gene, microbial

L112 ANSWER 25 OF 30 MEDLINE
ACCESSION NUMBER: 95353990 MEDLINE
DOCUMENT NUMBER: 95353990 PubMed ID: 7627817
TITLE: Ribozyme-mediated in vitro cleavage of transcripts arising from the major transforming genes of human papillomavirus type 16.
AUTHOR: Lu D; Chatterjee S; Brar D; Wong K K Jr
CORPORATE SOURCE: Division of Pediatrics, City of Hope National Medical Center, Duarte, California 91010, USA.
SOURCE: CANCER GENE THERAPY, (1994 Dec) 1 (4) 267-77.
Journal code: CE3; 9432230. ISSN: 0929-1903.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950921
Last Updated on STN: 19970203
Entered Medline: 19950907

AB Human papillomaviruses (HPV) have been strongly implicated as important cofactors in the development of several human malignancies, particularly anogenital carcinomas. Products arising from the E6 and E7 open reading frames (ORFs) from HPV-16, a type commonly associated with human cervical carcinoma, are essential for viral transformation. Unfortunately, a highly effective treatment for this infection is not available. To develop a novel treatment for this disease, ribozymes were designed to cleave all transcripts encoding HPV-16 E6 and E7 ORFs in proximity to their translational start sites ("AUG"). Cleavage sites for Rz110 and Rz558 occur immediately 3' to nucleotides 110 and 558 of the viral genomic DNA, respectively. Oligonucleotides corresponding to these ribozymes were synthesized and inserted into a eucaryotic viral vector derived from the nonpathogenic parvovirus, adeno-associated virus. Ribozyme transcription from this vector, termed CWRT7:SVN, is under control of both the highly active Rous sarcoma virus long terminal repeat and bacteriophage T7 promoters. T7 transcripts of the E6 and E7 ribozymes efficiently cleaved their cognate targets in vitro under a variety of conditions, including physiological temperature. These results may provide the basis for the development of a ribozyme-based, gene therapeutic treatment for HPV-associated diseases.

CT Check Tags: Human; Support, Non-U.S. Gov't
Bacteriophage T7: GE, genetics
Base Sequence
DNA, Recombinant: GE, genetics
DNA, Viral: GE, genetics
Dependovirus: GE, genetics
Drug Evaluation, Preclinical
s: GE, genetics
Therapy

Genetic Vectors: GE, genetics
Molecular Sequence Data
Nucleic Acid Conformation
Oligonucleotides, Antisense: GE, genetics
*Oncogene Proteins, Viral: GE, genetics
Open Reading Frames
Papillomavirus, Human
Papovaviridae Infections: TH, therapy
Promoter Regions (Genetics)
***RNA, Catalytic: PD, pharmacology**
RNA, Catalytic: TU, therapeutic use
*RNA, Messenger: ME, metabolism
*RNA, Viral: ME, metabolism
Sarcoma Viruses, Avian: GE, genetics
Substrate Specificity
Temperature
Transcription, Genetic
Tumor Virus Infections: TH, therapy

L112 ANSWER 26 OF 30 MEDLINE
ACCESSION NUMBER: 94014993 MEDLINE
DOCUMENT NUMBER: 94014993 PubMed ID: 8409934
TITLE: A recombinant retrovirus carrying a non-producer human immunodeficiency virus (HIV) type 1 variant induces resistance to superinfecting HIV.
AUTHOR: Federico M; Taddeo B; Carlini F; Nappi F; Verani P; Rossi G B
CORPORATE SOURCE: Laboratory of Virology, Istituto Superiore di Sanita, Rome, Italy.
SOURCE: JOURNAL OF GENERAL VIROLOGY, (1993 Oct) 74 (Pt 10) 2099-110.
Journal code: I9B; 0077340. ISSN: 0022-1317.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931116

AB A human immunodeficiency virus (HIV) type 1-infected Hut-78 cell clone (F12) shows a peculiar phenotype: it exhibits an altered viral protein pattern, is a nonproducer and is resistant to homologous superinfection. To determine whether this phenotype is dependent upon the expression of the HIV-1 genome integrated therein, the SstI/SstI F12 provirus [deprived of HIV long terminal repeats (LTRs)] was cloned and inserted in the pLj retroviral vector bearing the neomycin (neo) and Geneticin resistance gene. CD4+ HIV-susceptible CEMss cells (a CEM clone able to form large syncytia 2 to 3 days post-HIV infection) were infected with the recombinant retroviruses rescued from the F12/HIV-pLj-transfected (in either sense or antisense orientation) amphotropic packaging cells PA 317. Neo sense resistant gene clones showed approximately 10 copies of viral DNA/cell (without detectable major deletions) only in episomal form, low viral RNA expression and a viral protein pattern characterized by an uncleaved gp160, no gp41 and little, if any, p55 gag precursor (as in F12 cells). Superinfection of these F12/HIV DNA-engineered clones with HIV-1 resulted in a significant reduction in the yield of superinfecting HIV. This effect (more pronounced when the clones were maintained under neo selective pressure) was observed in all five retrovirus-infected clones exhibiting the presence and expression of sense episomal F12/HIV DNA but

not in two clones bearing an antisense F12/HIV DNA or in one clone bearing only the pLj vector. These results indicate that bio-engineered human CD4+ cells expressing the F12/HIV genome exhibit a significant resistance to HIV superinfection.

CT Check Tags: Human; Support, Non-U.S. Gov't
*Antigens, CD4: IM, immunology
*Antigens, Viral: IM, immunology
Base Sequence
Cells, Cultured
Cloning, Molecular
DNA, Viral: GE, genetics
Genetic Vectors
***HIV-1: IM, immunology**
Molecular Sequence Data
Plasmids
Polymerase Chain Reaction
*Recombinant Proteins: IM, immunology
Retroviridae
*Superinfection: IM, immunology
Transcription, Genetic
***Viral Interference: IM, immunology**

L112 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:208859 HCAPLUS
DOCUMENT NUMBER: 116:208859
TITLE: Cellular expression of a functional nodavirus RNA replicon from vaccinia virus vectors
AUTHOR(S): Ball, L. Andrew
CORPORATE SOURCE: Microbiol. Dep., Univ. Alabama, Birmingham, AL, 35294, USA
SOURCE: J. Virol. (1992), 66(4), 2335-45
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB RNA replication provides a powerful means for the amplification of RNA, but to date it has been found to occur naturally only among RNA viruses. In an attempt to harness this process for the amplification of heterologous mRNAs, both an RNA replicase and its corresponding RNA templates have been expressed in functional form, using vaccinia virus-bacteriophage T7 RNA polymerase vectors. Plasmids were constructed which contained in 5'-to-3' order (1) a bacteriophage T7 promoter; (2) a full-length cDNA encoding either the RNA replicase (RNA 1) or the coat protein (RNA 2) of flock house virus (FHV), (3) a cDNA sequence that encoded the self-cleaving ribozyme of satellite tobacco ringspot virus, and (4) a T7 transcriptional terminator. Both in vitro and in vivo, circular plasmids of this structure were transcribed by T7 RNA polymerase to produce RNAs with sizes that closely resembled those of the two authentic FHV genomic RNAs, RNA 1 and RNA 2. In baby hamster kidney cells that expressed authentic FHV RNA replicase, the RNA 2 (coat protein) transcripts were accurately replicated. Moreover, the RNA 1 (replicase) transcripts directed the synthesis of an enzyme that could replicate not only authentic virion-derived FHV RNA but also the plasmid-derived transcripts themselves. Under the latter **conditions**, **replicative** amplification of the RNA transcripts ensued and resulted in a high rate of synthesis of the encoded proteins. This successful expression from a DNA vector of the complex biol. process of RNA replication will greatly facilitate studies of its mechanism and is a major step towards the goal of harnessing RNA replication for mRNA amplification.

CT Gene, microbial

CT Replicon
CT Molecular cloning
CT Ribonucleic acids, messenger
CT Ribonucleic acids, viral
CT **Ribozymes**
CT Ribonucleic acids, viral
CT Ribonucleic acids, viral
CT Virus, bacterial
CT Proteins, specific or class
CT Virus, animal
CT Genetic element
CT Virus, plant
CT Genetic element
CT Virus, animal

L112 ANSWER 28 OF 30 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1990:21012638 BIOTECHNO
TITLE: Selective induction of toxicity to human cells expressing human **immunodeficiency** virus type 1 Tat by a conditionally cytotoxic adenovirus vector
AUTHOR: Venkatesh L.K.; Arens M.Q.; Subramanian T.; Chinnadurai G.
CORPORATE SOURCE: Molecular Virology Institute, Saint Louis University, Medical Center, 3681 Park Avenue,Saint Louis, MO 63110, United States.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1990), 87/22 (8746-8750) CODEN: PNASA6 ISSN: 0027-8424
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The human **immunodeficiency** viruses (**HIVs**) primarily infect CD4.sup.+ T lymphocytes, leading eventually to the development of a systemic immune dysfunction termed acquired **immunodeficiency** syndrome (AIDS). An attractive strategy to combat **HIV**-mediated pathogenesis would be to eliminate the initial pool of infected cells and thus prevent disease progression. We have engineered a **replication**-defective, **conditionally** cytotoxic adenovirus **vector**, Ad-tk, whose action is dependent on the targeted expression of the herpes simplex virus type 1 thymidine kinase gene (tk), cloned downstream of the **HIV**-1 long terminal repeat, in human cells expressing the **HIV**-1 transcriptional activator Tat. Infection of Tat-expressing human HeLa or Jurkat cells with Ad-tk resulted in high-level tk expression, which was not deleterious to the viability of these cells. However, in the presence of the anti-herpetic nucleoside analog ganciclovir, Ad-tk infection resulted in a massive reduction in the viability of these Tat-expressing cell lines. As adenoviruses are natural passengers of the human lymphoid system, our results suggest adenovirus vector-based strategies for the targeted expression, under the control of cis-responsive **HIV** regulatory elements, of cytotoxic agents in **HIV**-infected cells for the therapy of **HIV**-mediated pathogenesis.
CT *thymidine kinase; *adenovirus; *cytotoxicity; *human **immunodeficiency** virus 1; *virus infection; article; hela cell; human; priority journal

L112 ANSWER 29 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 86217005 EMBASE
DOCUMENT NUMBER: 1986217005

TITLE: Transformation of diploid human fibroblasts by DNA transfection with the v-sis oncogene.
AUTHOR: Fry D.G.; Milam L.D.; Maher V.M.; McCormick J.J.
CORPORATE SOURCE: Carcinogenesis Laboratory, Department of Microbiology, Michigan State University, East Lansing, MI 48824-1316, United States
SOURCE: Journal of Cellular Physiology, (1986) 128/2 (313-321). CODEN: JCLLAX
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
016 Cancer
LANGUAGE: English

AB The simian sarcoma virus (SSV) oncogene (v-sis) has a high degree of homology to the cellular gene coding for the B peptide of human platelet-derived growth factor (PDGF), a potent fibroblast mitogen. The cellular homolog of v-sis is activated in some mesenchymal human tumors and cell lines derived from them. To determine the phenotype produced by v-sis in diploid human fibroblasts, we constructed plasmids containing the SSV provirus and drug-resistance markers and transfected them into early-passage human cells. Fibroblasts that had integrated the plasmid were selected for drug resistance and shown to contain and express the v-sis oncogene by DNA and RNA hybridization. The v-sis-expressing cells grew to higher saturation densities than control cells transfected with the vector plasmid alone and formed large, well defined foci. This allowed selection of transfectants directly for focus formation. The v-sis transformed cells continued to grow well in the absence of serum, whereas age-matched, **vector**-transfected control cells ceased **replicating** under these **conditions** so that the final difference in density between the two populations was tenfold. Incorporation of thymidine in serum-free medium by the v-sis-transformed cells was independent of exogenous PDGF. In contrast, PDGF increased thymidine incorporation in such medium by the control cells to the level found in the v-sis-transformed cells with or without added PDGF. These results suggest that expression of the v-sis oncogene in diploid human fibroblasts causes sufficient endogenous synthesis of the B chain of PDGF to allow transformants to grow to abnormally high cell densities. When individual v-sis-transformed cells were grown on a background of normal cells, this higher cell density at confluence could be visualized as a focus.

CT Medical Descriptors:
*cell transformation
*dna transfection
*oncogene v sis
***simian sarcoma virus**
cell culture
diploid
fibroblast
priority journal
methodology
heredity
human cell
in vitro study
human

L112 ANSWER 30 OF 30 MEDLINE
ACCESSION NUMBER: 79237626 MEDLINE
DOCUMENT NUMBER: 79237626 PubMed ID: 381105
TITLE: A coliphage lambda vector with enhanced biological

containment: lambda gtALO.lambda B.
AUTHOR: Tabor J M; Bode V C
SOURCE: GENE, (1979 Apr) 5 (4) 255-74.
Journal code: FOP; 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197910
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19791026

AB The biological containment of the lambda gt family of cloning **vectors** has been enhanced by **conditionally** blocking DNA **replication** as well as head and tail morphogenesis. The vector, lambda gtALO.lambda B, was constructed by crossing the Oam29, Aama1 and Lam439 mutations into lambda gt.lambda B. The mutation blocking phage DNA replication, Oam29, is suppressed by suII+ or suIII+. The head gene mutation, Aama1, is suppressed by suIII+ but not by suII+ and the tail gene mutation, Lam439, is suppressed by suII+ but not by suIII+. This allows the option of increasing the biological containment by producing heads when a large amount of cloned DNA is being prepared from an individual isolate. A model recombinant, lambda gt Aama1 Lam439 Oam29.KmR' (lambda gtALO.KmR') was constructed and the containment of the vector was evaluated by the series of standardized experiments required for EK2 certification.

CT Check Tags: Comparative Study; Support, U.S. Gov't, P.H.S.
*Coliphages: GE, genetics
Crosses, Genetic
DNA Replication
DNA Restriction Enzymes
*DNA, Recombinant: ME, metabolism
DNA, Viral: BI, biosynthesis
Escherichia coli: GE, genetics
Genes, Viral
Genotype
Mutation
Species Specificity